AMENDMENTS TO THE CLAIMS

Claims 1-37 (Cancelled)

38. (New) A method for the in vitro modulation of the expression of a target gene in a cell population with an antisense oligomer said method characterised in that it comprises the step of inhibiting mature mRNA function of said target gene by contacting said cell population with an exon-bridging antisense oligomer directed against said mature mRNA of said target gene.

39. (New) The method of claim 38, wherein said exon-bridging antisense oligomer has a length of between 15-30 nucleotides.

40. (New) The method of claim 38, wherein the function of all mature mRNAs originating from said target gene is inhibited.

41. (New) The method of claim 38, wherein said exon-bridging antisense oligomer has a GC content of at least 45%.

42. (New) The method of claim 38, wherein the sequences complementary to the 5' and 3' end of the exon-exon boundary of said mRNA of said target gene have a Tm

of less than 32-36°C.

43. (New) The method of claim 38, wherein said exon-bridging antisense oligomer does not comprise a sequence of more than 11 consecutive nucleotides which are complementary to the sequence at the 3' end or the sequence at the 5' end of the exon-exon boundary in said mature mRNA of said target gene.

44. (New) The method of claim 38, which comprises contacting said cell population with I to 100 nM of said exon-bridging antisense oligomer.

45. (New) The method according to claim 38, wherein said target gene is IL1RI, said exon-bridging probe is an ILlRI exon-bridging antisense oligomer and wherein said modulation results in an increased synthesis of extracellular matrix compounds by said cell population.

46. (New) The method of claim 45, wherein said cell population is selected from the group consisting chondrocytes, chondrocyte precursors, fibrochondrocytes, fibroblasts or osteoarthritic chondrocytes.

47. (New) The method of claim 45, wherein said IL1RI exon-bridging antisense oligomer is complementary to a sequence bridging exons 02-03 in the mature mRNA of the IL1 RI gene.

48. (New) The method of claim 45, wherein said IL1RI exon-bridging antisense oligomer comprises a sequence between 15 and 30 nucleotides and does not comprise a sequence of more than 11 consecutive nucleotides which are complementary to the sequence at the 3' end or the sequence at the 5' end of the exon-exon boundary in the mature mRNA of the IL1 RI gene.

49. (New) The method of claim 45, wherein said IL1RI exon-bridging antisense oligomer is selected from a group consisting of probe NO:6 (SEQ ID NO:6), probe NO:7 (SEQ ID NO:7), probe NO:B (SEQ ID NO:8), probe NO:21 (SEQ ID NO:21) or a sequence having at least 70% sequence identity with the complementary sequence of the eDNA of the IL1 RI gene corresponding to said probes NO:6, NO:7, NO:8 or probe NO:21.

50. (New) The method of claim 45, wherein said IL1RI exon-bridging antisense oligomer comprises SEQ ID NO.7.

51. (New) The method of claim 45, wherein said IL1RI exon-bridging antisense oligomer is complementary to a sequence bridging oxen 05-06 of the mature mRNA of the IL1 RI gene.

52. (New) The method of claim 45, wherein said ILIRI exon-bridging antisense oligomer is selected from a group consisting of probe NO:24 (SEQ ID NO:24) or a sequence having at least 70% sequence identity with the complementary sequence of the eDNA of the IL1 RI gene corresponding to probe NO:24.

53. (New) An antisense oligomer for the inhibition of the expression of IL1RI characterised in that said antisense oligomer is an exon-bridging antisense oligomer.

54. (New) The antisense oligomer of claim 63, which is complementary to a sequence bridging exons 02M3 of the mature mRNA of the IL1 RI gene.

55. (New) The antisense oligomer of claim 53, which comprises a sequence between 15 and 30 nucleotides and does not comprise a sequence of more than 11 consecutive nucleotides which are complementary to the sequence at the 3' end or the sequence at the 5' end of the exon-exon boundary in the mature mRNA of the IL1 RI gene.

56. (New) The antisense oligomer of claim 53, wherein said IL1RI exon-bridging antisense oligomer is selected from a group consisting of probe NO:6 (SEQ ID NO:6), probe NO:7 (SEQ ID NO:7), probe NO:8 (SEQ ID NO:8), probe NO:21 (SEQ ID NO:21) or a sequence having at least 70% sequence identity with the complementary sequence of the cDNA of the IL1 RI gene corresponding to probes NO:6, NO:7, NO:8 or SEQ ID NO:21,

57. (New) The antisense oligomer of claim 53, wherein said IL1RI exon-bridging antisense oligomer comprises SEQ ID NO:7 or SEQ ID NO: 24.

58. (New) The antisense oligomer of claim 53, which is complementary to a sequence bridging exons 05-06 of the mature mRNA of the IL1RI gene.

59. (New) A pharmaceutical composition comprising one or more antisense oligomers according to claim 53 for the inhibition of the expression of IL1RI and further comprising at least one pharmaceutically acceptable carrier.

60. (New) A method for the treatment or prevention of a disease, selected from the group consisting of diseases characterized by a cartilage or osteochondral defect,

neuropathies, immune-mediated damage to the peripheral nervous system, heat hyperalgesia, Guillain-Barre syndrome, AIDS, bone disorders, bone resorption, coronary heart diseases, acute renal failure, asthma and nasal polyposis, said method comprising the step of administering one or more of the antisense oligomers according to claim 53.

61. (New) A method for producing an exon-bridging antisense oligomer for the inhibition of expression of a target gene comprising the steps of:

1) determining the exon-exon boundaries in the sequence of a spliced mRNA of said target gene,

2) selecting a sequence with a length between 15 and 30 residues bridging an exon-exon boundary in the spliced mRNA of said target gene, said sequence comprising at its 5' end or 3' end at least 4 residues identical to a sequence 5' of said exon-exon boundary and, optionally said sequence comprising at its 3' or 5' end a maximum of 11 residues identical to the sequence 3' adjacent of said exon-exon boundary.

3) producing an antisense oligomer which consists of a sequence which has at least 70% sequence identity with a sequence complementary to the sequence

selected in step 2.

62. (New) A method according to claim 61, wherein step 2 further comprises one or more of the steps selected from the group consisting of:

a) determining whether the GC content of said sequence determined under (2) is above 45 %,

b) determining whether the Tm of each of the sequences 3' and 5' of the exon-exon boundary within said sequence is below 32-36t.

c) determining whether said oligomer has a sequence identity below 70% with mature mRNA other than the mature mRNA or DNA of the target gene; and selecting the one or more sequences which fulfill the criteria of one or more of steps a to c.

63. (New) A method of treatment of a disease characterized by the overexpression of IL1RI, which comprises administering to a patient an exon-bridging antisense probe directed to mature mRNA of IL1 RI.